

average daily consumption of between about 18 and 36 mls of fluid per day of fluid. It will be appreciated that consumption the by very young mammals increases over time. The dosage to be administered is based on the measured sCD14 concentration in adult breast milk of 10 to 20 μg per ml, considering that a human infant increases its milk intake from about 0.1 l to about 1 l per day over the first six months after birth and assuming a weight ratio of about 28 between human and rat. In practice, particularly as human subjects are concerned, the daily dosage may well be from about 250 μg to about 2500 μg or more per kg of bodyweight per day. More preferably, the dosage would be in the neighborhood of from about 300 μg to about 1 mg per kg of bodyweight per day. It may be that the preferred frequency of administration would be greater or less than once per day, depending upon the route of administration, convenience, and the variation of effectiveness of treatment with frequency of and amount used per administration. The dosage administered also depends on the subject and to which effect such administration is to give. The dosage of any one or more of the compounds will depend on many factors including the specific compound or combination of compounds being utilized, the mode of administration, and the mammal being treated. Dosages of a particular compound or combination of compounds can be determined using conventional considerations; for example, by customary comparison of the differential activities of the subject compounds and that of a known agent, that is, by means of an appropriate pharmacological protocol.

IN THE SEQUENCE LISTING

Please insert the enclosed paper copy of the Sequence Listing on enclosed pages 1/9 to 9/9 into the application in place of the current Sequence Listing, which is hereby cancelled. A diskette containing the Sequence Listing in computer readable form is also enclosed.

IN THE CLAIMS

In accordance with 37 C.F.R. §1.121, please substitute following claims 159 to 195 for claims 1 to 158 of the application as filed, which claims are hereby cancelled.

159. A method of stimulating expression of at least one defensin in a mammal in need thereof, by administering a compound comprising soluble CD14 or a polypeptide portion of CD14 that enhances said expression, or a conservatively substituted variant of said CD14 or the portion that enhances said expression.

160. The method of claim 159, wherein said administering step includes directly exposing epithelial cells of the mammal to said compound.

161. The method of claim 160, comprising exposing the tongue and/or the gastrointestinal tract, optionally including the small intestine, of a said mammal to an effective amount of a said compound.

162. The method of claim 160, comprising exposing the respiratory tract of a said mammal to an effective amount of a said compound.

163. The method of claim 160, wherein the CD14 has an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and conservatively substituted variants of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7.

164. A method of ameliorating the symptoms of sepsis comprising administering to a mammal in need thereof an effective amount of a soluble protein so as to directly expose epithelial cells of the mammal to the protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:5 and having the ability to induce expression of defensins in epithelial cells.

165. The method of claim 164 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

166. A method of prophylactically treating a lipopolysaccharide-induced host inflammatory response in a mammal, which method comprises administering a therapeutically effective amount of an effective amount of a protein to the mammal so as to directly expose epithelial cells of the mammal to the protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to enhance expression of one or more defensins in bovine epithelial cells.

167. The method of claim 166 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or

about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

168. A method of enhancing expression of defensins in a mammal in need thereof, by administering an effective amount of a soluble protein to the mammal, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability enhance expression of defensins in mammalian epithelial cells.

169. The method of claim 168 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

170. The method of claim 159, wherein the compound comprises CD14 obtained from a mammalian mammary secretion.

171. The method of claim 170, wherein the CD14 is obtained from bovine milk.

172. The method of claim 170 wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of CD14 activity for inducing or stimulating defensin production in epithelial cells.

173. The method of claim 170, wherein the CD14 is contained in a liquid.

174. The method of claim 173, wherein the liquid comprises a fraction of the milk enriched in said CD14.

175. The method of claim 170, wherein said CD14 is contained in an edible product.

176. The method of claim 170, including administering the CD14 to the mammal orally.

177. A method for determining the suitability of a product derived from a mammary secretion for use in inducing or stimulating defensin production in mammals, the method comprising the steps of:

providing a sample of the product; and

determining the amount of CD14 present in the sample.

178. The method of claim 177, wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating said defensin production, and/or optionally, wherein determining the amount of CD14 present in the sample includes exposing the sample to an antibody which is specific for CD14, and ascertaining whether antibody-CD14 complex is formed in the exposing step.

179. The method of claim 176 wherein the compound is administered to an infant as a component of infant formula.

180. The method of claim 162 including administering the compound in the form of an aerosol.

181. A method of preparing a medicament, a dietary source or masticable product for use in directly stimulating defensin production in a mammal, method comprising the steps of:

providing a stock solution containing protein of a mammary secretion;

separating, optionally precipitating, from the solution a concentrate comprising endogenous CD14; and

determining the concentration of CD14 in the concentrate,

wherein, the mammary secretion can comprise milk, whole milk, a protein-containing portion of whole milk, or colostrum, and/or

wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating defensin production.

182. The method of claim 181, wherein the mammary secretion is bovine.

183. The method of claim 181, wherein the solution is a liquid solution and the separating step includes salting out of proteins from the solution, and optionally, wherein determining the concentration of CD14 includes exposing a sample obtained from the concentrate to a first antibody specific for CD14 to form an antibody-CD14 complex and subsequently exposing the complex to a second antibody specific for CD14, wherein the second antibody includes a reporter molecule,

wherein determining the concentration of CD14 can include exposing a sample obtained from the concentrate to a first antibody specific for CD14 to form an antibody-CD14 complex and subsequently exposing the complex to a second antibody specific for the first antibody, wherein the second antibody includes a reporter molecule.

184. The method of claim 181, wherein the precipitating step includes increasing the salt concentration of the solution to obtain an ionic strength at least as high as would be obtained by combining a saturated aqueous solution of ammonium sulphate with a volume of a said mammary secretion, the volume of the ammonium sulphate solution being equal to 65 percent of the total volume of the combined solutions.

185. The use of a mammary secretion in a method of preparing a medicament, a dietary source or masticable product for use in directly stimulating defensin production in a mammal, method comprising the steps of:

providing a composition containing protein of the mammary secretion;
exposing the composition to an antibody which is specific for CD14; and
determining whether CD14 endogenous to the secretion is present in the sample based on whether CD14-antibody complex has formed in the exposing step.

186. The method of claim 185 wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating defensin production, optionally comprising the further step of determining the concentration of CD14 in the sample.

187. The method of claim 159, wherein the polypeptide is contained in concentrated milk.

188. The method of claim 159, including the step of direct topical exposure of the epithelium of the trachea to the polypeptide or protein, as the case may be.

189. The method of claim 159, including the step of topical exposure to the outer epidermis of a mammal, particularly to wounds thereof.

190. A method of preparing an ointment for direct topical application to a wound of human skin for ameliorating the effects of infection, particularly bacterial infection, thereof, comprising incorporating into the ointment an effective amount of a concentrate comprising CD14 obtained from a mammary secretion, or a polypeptide of claim 159.

191. A dietary source such as infant formula, milk or other liquid having added thereto a fraction of a milk product, the fraction including a higher concentration of CD14 than occurs naturally in the unfractionated milk product, wherein the milk product is one which has not been treated by a process which denatures the CD14 contained therein to the extent that CD14 loses the desired activity, particularly the ability to stimulate defensins in epithelial cells.

192. The method of claim 166, wherein the mammal is in need of protection against a microbial pathogen selected from the group consisting of virus, bacteria, fungus and yeast.

193. The method of claim 159, where the mammal a human suffering from immune deficiency.

194. The method of any of claims 159, wherein the defensin(s) is selected from the group consisting of RtNP1, RtNP2, RtNP3, RtNP4, HNP1, HNP2, and HNP3 and any combination thereof, or the group consisting of HNP1, HNP2, and HNP3.